

## REMARKS

### ***Status of the Claims***

Claims 1-46 are pending, with claims 1-20, 22-28, 32-34, 38 and 41 having been withdrawn from consideration. Non-withdrawn claims 22 and 35 are independent. Claims 21 and 22 are amended herein. In particular, claim 21, previously dependent on withdrawn claim 12, has been amended to depend from claim 35. Claim 22 has been amended to replace "screening nucleation tendency of a molecule in a fluid" with "screening crystallization conditions or amorphous stage conditions of a molecule". No new matter has been added.

Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections in view of the foregoing amendments and following remarks.

### **Claim Objections**

Claim 21 stands objected as it allegedly depends from a withdrawn claim. Claims 29-31 are also included under this objection due to their dependence from claim 21. Without conceding the propriety of the objection, claim 21 has been amended to depend from claim 35. Accordingly, withdrawal of this objection is respectfully requested.

### **Rejections Under 35 U.S.C. § 103**

Claims 21, 29, 30, 35-37, 40, 44, and 45 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over "Development of Acoustic and Electrostatic Levitators for Containerless Protein Crystallisation", *Sci. Tech. J.*, December 1993; 29(4):330-338 ("Ishikawa") in view of "Accurate high-speed liquid handling of very

small biological samples", *Biotechniques*, August 1993; 15(2):324-329 ("Schober") in further view of "Supersaturated electrolyte solutions: Theory and Experiment", *Physical Review E*, October 1995, 52(4):3923-3935 ("Izmailov"). Applicants disagree with this rejection; therefore, this rejection is traversed.

Ishikawa discloses doing protein crystallization experiments on lysozyme using an acoustic levitator to determine whether the levitator influences crystal growth. (Abstract). Ishikawa discloses, "With the acoustic levitator, crystals did not form in any solution. This suggests that acoustic vibration affects crystallization. . . . [I]t seems that vibration-induced streaming within the droplet prevented crystallization." (Page 337, Column 1). The Office Action acknowledges that Ishikawa does not disclose delivering at least one substance to the levitating droplet. (Page 5).

Schober describes "a technique for the accurate microdispensation of biochemically relevant solutions and suspensions with the aid of a piezoelectric transducer." (Abstract). The Office Action acknowledges that Schober does not teach the delivery of substances from a piezoelectric dispenser to a levitated droplet. (Page 6).

Izmailov discloses preparing and studying highly supersaturated electrolyte solutions employing an electrodynamic levitator trap (ELT) technique. (Abstract). The Office Action asserts that Izmailov employs "a piezoelectric dispenser to deliver highly accurate volumes of microdroplets to a sample droplet levitated in the center of a spherical void electromagnetic levitator trap (SVELT) in order to investigate homogeneous nucleation conditions." (Page 6). Applicants respectfully submit that there is no suggestion or disclosure that the piezoelectric ceramic shown in Figure 1

of Izmailov is a dispenser for delivery of microdroplets to a levitated sample droplet.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2143.

Applicants submit that these criteria have not been met.

#### Independent Claim 22

Amended independent claim 22 recites a method for screening crystallization conditions or amorphous stage conditions of a molecule, comprising levitating at least one droplet of said fluid in an ultrasound acoustic levitator. At least one substance is delivered to said levitating droplet with a dispenser for delivering said substance. The nucleation tendency is detected by multi-angle light scattering in combination with Raman spectroscopy to obtain a quantitative measurement of turbidity, precipitate, and/or aggregate formation in said at least one droplet, while the concentrations of substances in said levitated droplet is gradually increased over time by means of either droplet evaporation or addition of precipitants and utilizing the vibration-induced streaming caused by ultrasound to further the precipitation in said droplet. The nucleation tendency is scored.

Applicants respectfully submit that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the cited references; nor is there a reasonable

expectation of success; and the prior art references when combined do not teach or suggest all the claim limitations.

Following the assertion in the Office Action that Izmailov employs a piezoelectric dispenser to deliver highly accurate volumes of microdroplets to a sample droplet levitated in the center of a SVELT, the Office Action contends that "it would have been obvious to one of skill in the art to employ a piezoelectric transducer device to accurately deliver substances to the levitated droplet in the methodology and system as disclosed by Ishikawa." (Page 6). As noted above, the Office Action acknowledges that Ishikawa does not disclose delivering at least one substance to the levitating droplet and that Schober does not teach the delivery of substances from a piezoelectric dispenser to a levitated droplet and Applicants respectfully submit that Izmailov does not disclose or suggest a piezoelectric dispenser to deliver microdroplets to a levitated sample droplet. Accordingly, Applicants respectfully submit that the Office Action has failed to provide any suggestion or motivation to combine Ishikawa, Schober, and Izmailov to employ a dispenser to deliver substances to a levitated droplet.

As there is no suggestion or motivation to combine Ishikawa, Schober, and Izmailov, there is similarly no reasonable expectation of success to employ a dispenser to deliver substances to a levitated droplet.

Additionally, Applicants respectfully submit that the combination of Ishikawa, Schober, and Izmailov does not disclose or suggest all the claim limitations. In particular, the combination of Ishikawa, Schober, and Izmailov does not disclose or suggest: (1) delivering at least one substance to a levitating droplet; (2) detecting the nucleation tendency by multi-angle light scattering in combination with Raman

spectroscopy to obtain a quantitative measurement of turbidity, precipitate, and/or aggregate formation in at least one droplet, while the concentrations of substances in the levitated droplet is gradually increased over time by means of either droplet evaporation or addition of precipitants and utilizing the vibration-induced streaming caused by ultrasound to further the precipitation in the droplet; or (3) scoring the nucleation tendency.

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). MPEP § 2141.02.

Applicants respectfully submit that Ishikawa, which discloses that vibration-induced streaming within the droplet in an acoustic levitator prevents crystallization, teaches away from the presently claimed method for screening crystallization conditions or amorphous stage conditions of a molecule which recites, *inter alia*, “utilizing the vibration-induced streaming caused by ultrasound to further the precipitation in the droplet.”

#### Independent Claim 35

Independent claim 25 recites a system for screening crystallization conditions or amorphous stage conditions of a molecule, comprising at least one levitator for positioning at least one droplet, at least one dispenser for delivering at least one substance to the positioned droplet, and one or more means for detecting nucleation tendency in the at least one levitated droplet.

Applicants respectfully submit that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the cited references nor is there a reasonable expectation of success

As noted above, Applicants respectfully submit that the Office Action has failed to provide any suggestion or motivation to combine Ishikawa, Schober, and Izmailov and accordingly, there is no reasonable expectation of success to employ a dispenser to deliver substances to a levitated droplet.

For at least the above-noted reasons, withdrawal of this rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claims 31, 42, and 46 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ishikawa in view of Schober in further view of Izmailov and further in view of U.S. Patent Application Publication No. 2004/0033166 ("Arnowitz").

Applicants disagree with this rejection; therefore, this rejection is traversed.

Arnowitz is cited in the Office Action as disclosing methods and systems for controlling dynamic, reagent induced transformations of multiple biological samples being crystallized. (Pages 7 and 8).

Applicants respectfully submit that Arnowitz does not cure the above-noted deficiencies with regard to the combination of Ishikawa, Schober, and Izmailov.

For at least the above-noted reasons, withdrawal of this rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claims 39 and 34 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ishikawa in view of Izmailov in view of Schober in further view of Arnowitz and further in view of "The use of Raman spectroscopy for in situ monitoring of lysozyme concentration during crystallization in a hanging drop", *J. Cryst. Growth*, 1999; 203:599-603 ("Schwartz"). Applicants disagree with this rejection; therefore, this rejection is traversed.

Schwartz is cited in the Office Action as disclosing the use of Raman spectroscopy for monitoring protein concentration to report on nucleation condition of a sample being crystallized. (Page 9).

Applicants respectfully submit that Schwartz does not cure the above-noted deficiencies with regard to the combination of Ishikawa, Schober, Izmailov, and Arnowitz.

For at least the above-noted reasons, withdrawal of this rejection under 35 U.S.C. § 103(a) is respectfully requested.

**CONCLUSION**

In view of the foregoing amendments and remarks, reconsideration of the claims and allowance of the subject application is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

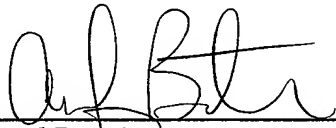
In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL PC

Date: 9/13/09

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